

Appl. No. : 09/996,020 Appl. No. : 09/996,020
Filed : November 27, 2001

In the Claims

Please amend claims 45 and 100 as follows:

1-29 (Cancelled)

30-44 (Withdrawn)

45. (Currently amended) Method for the formation of a particulate product comprising: co-introducing through respective inlet passages a flow of a supercritical fluid and a flow of a vehicle containing at least one substance into a particle formation vessel, wherein the flows of the supercritical fluid and the vehicle containing the substance both enter the vessel from said passages at the same location which is substantially the same as the location at which they meet, the inlet passages are further arranged such that the flow of supercritical fluid is used to disperse the vehicle containing the substance and that the supercritical fluid can simultaneously extract the vehicle from the substance at the location where the fluids meet.

46. (Previously added) Method according to claim 45 further comprising controlling the temperature and pressure within the particle formation vessel.

47. (Previously added) Method according to claim 45, wherein the co-introduction of the supercritical fluid and the vehicle is effected using a coaxial nozzle the outlet end of which communicates with the interior of the particle formation vessel, the nozzle having coaxial passages which terminate adjacent to one another at the outlet end, at least one of the passages serving to carry a flow of the supercritical fluid, and at least one of the passages serving to carry a flow of the vehicle.

48. (Previously added) Method according to claim 45 wherein the substance is in solution in the vehicle.

49. (Previously added) Method according to claim 45 wherein the substance is suspended in the vehicle.

Appl. No. : 09/996,020 Appl. N. : 09/996,020
Filed : November 27, 2001

50. (Previously added) Method according to claim 45, wherein the supercritical fluid is carbon dioxide.

51. (Previously added) Method according to claim 45, wherein the supercritical fluid contains one or more modifiers.

52. (Previously added) Method according to claims 45, wherein the product to be formed is a pharmaceutical compound.

53. (Previously added) Method according to claims 45, additionally comprising the controlling the flow rate of the supercritical fluid and the vehicle; the concentration of the substance(s) in the vehicle; and the temperature and pressure inside the particle formation vessel.

54. (Previously added) Method according to claims 45, wherein the pressure in the particle formation vessel is maintained substantially in excess of the critical pressure for the supercritical fluid, whilst the temperature in the vessel is maintained at slightly above the critical temperature for the supercritical fluid.

55. (Previously added) Method according to claim 45, wherein the ratio of the vehicle flow rate to the supercritical fluid flow rate is between 0.001 and 0.1.

56. (Previously added) Method according to claim 45, additionally comprising the step of recovering and recycling the vehicle and the supercritical fluid following particle formation.

57. (Previously added) A method for forming particulates comprising a substrate surrounded by a coating layer comprising:

contacting a coating material and a substrate with a supercritical fluid upon co-introduction into a particle formation vessel.

58. (Previously added) A method according to claim 57 wherein said coating material is

Appl. No. : 09/996,020 Appl. No. : 09/996,020
Filed : November 27, 2001

provided as a solution or suspension in a first vehicle.

59. (Previously added) A method according to claim 58 wherein said substrate is provided as a dispersion in a second vehicle.

60. (Previously added) A method according to claim 59 wherein the coating material is in solution.

61. (Previously added) A method according to claim 59 wherein the coating material is suspended in the first vehicle.

62. (Previously added) A method according to claim 59 wherein the first and second vehicles are provided separately to the particle formation vessel.

63. (Previously added) A method according to claim 59 wherein the co-introduction is such that the flow of supercritical fluid can simultaneously extract the first and second vehicles.

64. (Previously added) Method according to claim 63, wherein the co-introduction is effected using a coaxial nozzle the outlet end of which communicates with the interior of the particle formation vessel, the nozzle having coaxial passages which terminate adjacent to one another at the outlet end, at least one of the passages serving to carry a flow of the supercritical fluid.

65. (Previously added) A method according to claim 59, wherein the supercritical fluid, the solution or suspension and the second vehicle are co-introduced into the particle formation vessel by a nozzle having an outlet end communicating with the interior of the particle formation vessel, and two or more coaxial passages which terminate adjacent or substantially adjacent to one another at the outlet end, at least one of the passages serving to introduce a flow of the supercritical fluid into the particle formation vessel, at least one of the passages serving to introduce a flow of the solution or suspension of the substance in the first vehicle and at least one of the passages serving to introduce a flow of the second vehicle.

Appl. No. : 09/996,020 Appl. No. : 09/996,020
Filed : November 27, 2001

66. (Previously added) A method according to claim 65, wherein the solution or suspension of the substance in the first vehicle is introduced into the particle formation vessel through one passage of the nozzle, and the supercritical fluid and the second vehicle are introduced together through another passage of the nozzle, and mixing of the two vehicles occurs substantially simultaneously with their dispersion and extraction by the supercritical fluid.

67. (Previously added) A method according to claim 66, wherein the nozzle has at least three coaxial passages, the solution or suspension being introduced between an inner and an outer flow of the supercritical fluid/second vehicle mixture.

68. (Previously added) A method according to claim 65, wherein the nozzle has at least three coaxial passages, the outlet of at least one of the inner nozzle passages being located a small distance upstream of the outlet of one of its surrounding passages, the distance being sufficient to allow a degree of pre-mixing to occur between fluids introduced through said inner and surrounding passages, and wherein the solution or suspension and the second vehicle are introduced through the inner passage and surrounding passage in question so as to allow, in use, a degree of mixing to occur, between the solution or suspension and the second vehicle, within the nozzle.

69. (Previously added) A method according to claim 68, wherein the nozzle has at least four coaxial passages, and wherein the solution or suspension and the second vehicle are introduced into the particle formation vessel between an inner and an outer flow of the supercritical fluid.

70. (Previously added) A method according to claim 63 wherein the temperature and pressure within the particle formation vessel are controlled.

71. (Previously added) A method according to claim 70, wherein the pressure in the particle formation vessel is maintained substantially in excess of the critical pressure for the supercritical fluid, whilst the temperature in the vessel is maintained at slightly above the critical temperature for the supercritical fluid.

Appl. No. : 09/996,020 Appl. No. : 09/996,020
Filed : November 27, 2001

72. (Previously added) A method according to claim 59 wherein said substrate comprises a pharmaceutically active agent.

73. (Previously added) A method according to claim 59 wherein said substrate comprises a pharmaceutically acceptable carrier.

74. (Previously added) A method according to claim 73 wherein said coating material comprises a pharmaceutically active agent.

75. (Previously added) A method according to claim 72 wherein said coating material comprises a pharmaceutically acceptable carrier.

76. (Previously added) A method according to claim 75 wherein said carrier comprises a taste-masking agent.

77. (Previously added) Method according to claim 57, wherein the supercritical fluid is carbon dioxide.

78. (Previously added) Method according to claim 57, wherein the supercritical fluid contains one or more modifiers.

79. (Previously added) Method according to claim 58, additionally comprising the control of the concentration of the substance(s) in the vehicle.

80. (Previously added) A method according to claim 59, wherein a flow rate of the second vehicle into the particle formation vessel is greater than that of the solution or suspension.

81. (Previously added) A method according to claim 80, wherein the ratio of the solution/suspension flow rate, into the particle formation vessel, to that of the supercritical fluid is between 0.001 and 0.2.

Appl. No. : 09/996,020 Appl. No. : 09/996,020
Filed : November 27, 2001

82. (Previously added) A method according to claim 59, wherein the amount of the first vehicle used is less than or equal to about 30% of the total amount of the first and second vehicles used.

83. (Previously added) A method according to claim 59, wherein one of the two vehicles contains functional groups that may interact, through hydrogen-bonding or dipole-dipole interactions, with functional groups contained in the other vehicle.

84. (Previously added) A method according to claim 59, wherein the substance and the first vehicle are substantially polar and the second vehicle is substantially non-polar.

85. (Previously added) A method according to claim 59, wherein the substance and the first vehicle are substantially non-polar and the second vehicle is substantially polar.

86. (Previously added) A method according to claim 59 wherein the substance is substantially insoluble in the second vehicle.

87. (Previously added) A method in accordance to claim 59, wherein the second vehicle contains a crystallization seed of a material which is insoluble in the second vehicle to induce nucleation of the substance when the second vehicle comes into contact with the solution or suspension of the substance in the first vehicle.

88. (Previously added) A method in accordance to claim 87, wherein the substance is a pharmaceutical substance, and the seed comprises a pharmaceutically acceptable carrier for the substance.

89. (Previously added) A method according to claim 57, which is carried out in a plural batch manner by switching between two or more particle formation vessels or between two or more means for collecting the particulate product.

Appl. No. : 09/996,020 Appl. No. : 09/996,020
Filed : November 27, 2001

90. (Previously added) A method for forming particulates comprising a substrate surrounded by a coating layer comprising:

contacting a first vehicle containing a coating material and a second vehicle containing a substrate with a supercritical fluid.

91. (Previously added) A method according to claim 90 wherein the contacting step comprises co-introduction of the first vehicle, second vehicle, and supercritical fluid into a particle formation vessel.

92. (Previously added) A method according to claim 91 wherein the first and second vehicles and supercritical fluid are co-introduced such that the flow of supercritical fluid can simultaneously extract the first and second vehicles.

93. (Previously added) A method according to claim 91 wherein the first vehicle contains a solution or suspension of the coating material and the second vehicle contains a dispersion of the substrate.

94. (Previously added) A method according to claim 93 wherein the first and second vehicles and supercritical fluid are introduced separately into the vessel.

95. (Previously added) A method according to claim 93 wherein said substrate comprises a pharmaceutically active agent.

96. (Previously added) A method according to claim 93 wherein said substrate comprises a pharmaceutically acceptable carrier.

97. (Previously added) A method according to claim 96 wherein said coating material comprises a pharmaceutically active agent.

98. (Previously added) A method according to claim 95 wherein said coating material comprises a pharmaceutically acceptable carrier.

Appl. No. : 09/996,020 Appl. No. : 09/996,020
Filed : November 27, 2001

99. (Previously added) A method according to claim 98 wherein said carrier comprises a taste-masking agent.

100. (Currently amended) A method for forming particulates comprising a substrate surrounded by a

coating layer comprising:

controlling the temperature and pressure within a particle formation vessel; and contacting a flow of a first vehicle containing a coating material and a flow of a second vehicle containing a substrate with a supercritical fluid upon co-introduction into the particle formation vessel such that the flow of supercritical fluid can simultaneously extract the first and second vehicle.

101. (Previously added) A method according to claim 100 wherein said first vehicle contains a solution or suspension of the coating material and the second vehicle contains a dispersion of the substrate.

102. (Previously added) A method according to claim 101 wherein said substrate comprises a pharmaceutically active agent.

103. (Previously added) A method according to claim 101 wherein said substrate comprises a pharmaceutically acceptable carrier.

104. (Previously added) A method according to claim 103 wherein said coating material comprises a pharmaceutically active agent.

105. (Previously added) A method according to claim 102 wherein said coating material comprises a pharmaceutically acceptable carrier.

106. (Previously added) A method according to claim 105 wherein said carrier comprises a

Appl. No. : 09/996,020 Appl. No. : 09/996,020
Filed : November 27, 2001

taste-masking agent.

107. (Previously added) A method for separating isomers comprising:
contacting a mixture of isomers in a first vehicle with a supercritical fluid upon co-introduction into a particle formation vessel.
108. (Previously added) A method according to claim 107 wherein the isomer mixture and supercritical fluid are co-introduced such that the flow of supercritical fluid can simultaneously extract the first vehicle.
109. (Previously added) Method according to claim 107 further comprising controlling the temperature and pressure within the particle formation vessel.
110. (Previously added) Method according to claim 107, wherein the co-introduction of the supercritical fluid and the vehicle is effected using a coaxial nozzle the outlet end of which communicates with the interior of the particle formation vessel, the nozzle having coaxial passages which terminate adjacent to one another at the outlet end, at least one of the passages serving to carry a flow of the supercritical fluid, and at least one of the passages serving to carry a flow of the vehicle.
111. (Previously added) Method according to claim 110, wherein the pressure in the particle formation vessel is maintained substantially in excess of the critical pressure for the supercritical fluid, whilst the temperature in the vessel is maintained at slightly above the critical temperature for the supercritical fluid.
112. (Previously added) Method according to claim 107, wherein the ratio of the vehicle flow rate to the supercritical fluid flow rate is between 0.001 and 0.1.
113. (Previously added) Method according to claim 107 further comprising co-introducing a second vehicle

Appl. No. : 09/996,020
Filed : November 27, 2001

114. (Previously added) A product made by the process of any one of claims 45-47, 52-55, 57-66, 70-76, 80-82, 87, 88, 90, 100 or 107-113.

115. (Previously added) A product according to claim 114 in a single polymorphic form.

116. (Previously added) A product according to claim 114 in a single isomeric form.

117. (Previously added) A product according to claim 114 comprising a multi-component particulate.

118. (Previously added) A product according to claim 114 comprising a protein.

119. (Previously added) A product according to claim 114 comprising a sugar.

120. (Previously added) A product according to claim 114 in amorphous form.

121. (Previously added) A product according to claim 114 comprising a substrate provided with a coating.

122. (Previously added) A product according to claim 114 in crystalline form

123. (Previously added) A method according to any one of claims 115-122 further comprising administering the particulates by inhalation.